

Quality Management Plan

Biological and Economic Analysis Division
Microbiology Laboratory Branch

Office of Pesticide Programs

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A. Program Overview

The primary focus of the Office of Pesticide Program's (OPP), Biological and Economic Analysis Division (BEAD), Microbiology Laboratory Branch (MLB) is centered on the efficacy of antimicrobial products with public health claims that are registered by the EPA— products used to kill or suppress the growth of infectious microorganisms on inanimate objects and surfaces. MLB is located at Environmental Science Center, Fort Meade, MD. Applied research on the evaluation and development of methods used to determine the efficacy of antimicrobials is a key priority. Recently, the laboratory has expanded its services to include, among others, major research effort in response to the anthrax attacks per the Homeland Security priorities of the Office of Research and Development's National Homeland Security Research Center and Office of Pesticide Programs and Toxic Substances (OPPTS), and work on methods to identify genetically modified plant material.

I. Antimicrobial Testing Program (ATP)

This program was initiated in response to findings presented by the Government Accounting Office (GAO) that the EPA lacked assurance that antimicrobial products registered by the Agency were efficacious. EPA has focused its efforts on evaluating registered products that are most crucial to infection control (sterilants, tuberculocides, and hospital-level disinfectants). The manufacturer of any product bearing a public health claim is required to submit efficacy data to the Antimicrobials Division (AD) of OPP to substantiate the product's effectiveness and AD evaluates and registers antimicrobials. OPP's Microbiology Laboratory Branch, in conjunction with certain state laboratories, perform efficacy tests using the same parameters (contact time, dilution of product) as noted on the product label. If testing demonstrates that a product does not provide acceptable levels of control of target microorganisms, EPA's Office of Regulatory Enforcement takes action against the manufacturer. The Agency has completed testing of sterilant products, and is currently testing approximately 800 EPA-registered hospital-level disinfectants and 150 tuberculocides. Standard Operating Procedures (SOPs) used by the OPP Microbiology Laboratory to determine the efficacy of hard surface disinfectants against infectious microorganisms are found at <http://www.epa.gov/oppbead1/methods/atmpindex.htm>

II. Plant Incorporated Protectant (PIP) Method Validation Program

EPA regulates Plant Incorporated Protectants – materials that enable a plant to protect itself from pests such as insects, viruses and fungi by producing its own pesticide. The Biopesticides and Pollution Prevention Division (BPPD) is responsible for regulating PIPs. A PIP plant in the field, however, cannot be distinguished visually from a conventional plant. So, current PIP registration guidelines require registrants to submit a method for the detection of the unique PIP DNA sequence, as well as a method to detect the protein expressed by that unique DNA sequence. OPP's Microbiology Laboratory validates detection methods submitted with registration applications.

III. Homeland Security Research

OPP has the responsibility for regulating antimicrobial products, including sporicides, used to treat and decontaminate inanimate surfaces. BEAD's Microbiology Laboratory Branch (MLB) is responsible for conducting testing of antimicrobial products to ensure products are effective and to guard against manufacturer's false claims (core program activities). The Laboratory's resources and expertise are also well suited to meet the increased Homeland Security need for improved and standardized efficacy test methods to ensure that decontamination products are effective in inactivating bioterrorism agents.

Homeland Security Presidential Directive 10 directs EPA to take the federal lead for "developing specific standards, protocols, and capabilities to address the risks of contamination following a biological weapons attack and developing strategies, guidelines, and plans for decontamination of persons, equipment, and facilities." EPA's Office of Prevention, Pesticides, and Toxic Substances (OPPTS) has taken action to address this directive and significantly improve the nation's ability to treat contaminated sites and to allow for safe re-occupancy. Developing proven standard methods for evaluating and testing the effectiveness of antimicrobial decontamination products, such as those used to decontaminate facilities contaminated in 2001 with spores of *Bacillus anthracis* (anthrax) is critical for protecting public health. Standardizing protocols and harmonizing testing activities across the federal agencies are common themes throughout the overall OPP antimicrobial testing program. BEAD's MLB is the lead OPP research organization involved in this effort. OPP seeks the input and interaction from scientists and officials from other federal agencies and through participation on multiple working groups (e.g., Interagency Expert Panel on Anthrax, AOAC Expert Review Panel roundtables with industry stakeholders). The current work on anthrax spore decontamination test methods has set the stage for research and the development of regulatory guidance for other threat agents and emerging pathogens.

Research associated with spore-formers and liquid decontamination agents on hard surfaces was the initial priority; however, additional threat agents [*Yersinia pestis* (plague) and *Francisella tularensis* (tularemia)], carrier surface materials (e.g. porous building materials), and product formulations (e.g. gases) have been added to the research initiative. Through funding provided by EPA's Office of Research and Development (FY04 – FY06) and OPPTS (FY05-FY07), a multi-tiered research plan was developed and initiated. Interagency Agreements (IAGs) were established with federal research partners (Department of Defense and the Food and Drug Administration) to assist EPA in this effort. AOAC International, a standard-setting organization, was also funded to provide third-party review and oversight. Research projects conducted under this program include the comparative evaluation of quantitative test methods for liquid sporicides, collaborative testing of selected modifications to improve the Agency's current reference method, AOAC Method 966.04 (Sporicidal Activity of Disinfectants Test), the evaluation of surrogates of *B. anthracis* using a quantitative method, and a multi-laboratory validation study of a quantitative method (Three Step Method) for liquid sporicides on a hard surface. Ultimately, the data and study conclusions will be used to develop/supplement regulatory guidelines for decontamination products to be used in the treatment of buildings and

environmental surfaces.

IV. Center for Disease Control (CDC) Select Agent Laboratory

The OPP Microbiology Laboratory has obtained full registration under the CDC Select Agent Rule (Public Health Security and Bioterrorism Preparedness and Response Act of 2002). The laboratory is considering joining the CDC Laboratory Response Network (LRN), a nationwide laboratory network for food, veterinary, plant health, and water quality that integrates existing Federal and State laboratory resources and standardizes diagnostic protocols and procedures. The LRN deals primarily with public health needs. As a referral laboratory within the LRN, the Microbiology Laboratory would be limiting its work to analysis of *Bacillus anthracis* environmental samples.

Additional Functions

1. Operate a pre-registration testing program to verify selective antimicrobial efficacy claims and assure the quality and integrity of registrant-submitted data.
2. Serve as a source of technical information regarding test methodology to referee disputes, and confirm test sample results from state government laboratories.
3. Provide technical and training support to state laboratories.
4. Carry out development of new antimicrobial test methods, including the evaluation of potential screening or rapid methods.
5. Participate in collaborative ("round robin") efficacy testing of new test methods for evaluating antimicrobial products.
6. Participate in data audits and GLP inspections of commercial/industrial labs which conduct efficacy testing of disinfectants and antimicrobial devices.
7. Serve as expert witness in Agency conducted hearings.

The client base includes the Antimicrobials Division (AD), the Biopesticides and Pollution Prevention Division (BPPD), and the EPA Office of Research and Development (ORD) and other government and state Agencies. Core program work is conducted in consultation with the client. Review and signature of the study protocols is at the client level.

B. MANAGEMENT AND ORGANIZATION

I. General Organizational Structure

The general organization structure of the Office of Pesticide Programs and Biological and

Economic Analysis Division is included in Appendices A-1 thru A-4.

II. Mission

The mission of the program office is the regulation and oversight of pesticide products. The overarching theme of work underway at the laboratory is to provide microbiological laboratory support to the Office of Pesticide Programs. The focus of the programs at the laboratory change as OPP's needs change. In recent years, the focus has been on the efficacy evaluation of antimicrobials, efficacy method development and modifications, particularly for sporicidal chemicals, method validations for PIPs, and research related to the ATP initiatives. Mission program support for the efficacy evaluations of tuberculocides and hospital disinfectants is also provided by three state laboratories.

III. Policy on Quality Assurance

The goal of the Agency-wide Quality System is to ensure that environmental programs and decisions are supported by data of the type and quality needed and expected for their intended use. The objectives of the Good Laboratory Practices (GLP) program, quality assurance (QA) program, and quality control (QC) checks are to ensure the validity and accuracy of the data.

Standard Operating Procedures (SOPs) form the basis for work at the laboratory. Protocols are written for individual studies; overall QA elements are identified in Quality Assurance Project Plans (QAPPs). The laboratory conforms to the (GLP) Standards outlined in 40 CFR Part 160. A schedule is followed for review and amendment of SOPs. An audit schedule is developed each year and includes internal technical system audits, books and records audits, and audits of individual studies. The laboratory is also subject to external technical and management systems audits which serve to identify any deficiencies in the quality assurance programs.

IV. Responsibilities

Agency policy mandates that the laboratory operate in conformance with GLPs. This requires the laboratory to utilize a prescribed quality assurance program with thorough documentation of all quality control activities. Senior management is responsible for allocating resources and support to the Quality Assurance Officer (QAO) as necessary to implement the recommended quality assurance activities of the laboratory. The Branch Chief is responsible for ensuring that corrective action is taken to address deficiencies noted during audits of laboratory data or practices.

All staff involved in conducting laboratory assessments are responsible for ensuring that required quality control measures are carried out as prescribed in the SOPs. Laboratory staff are responsible for the intra-laboratory review of data generated under the program.

The laboratory has an assigned Quality Assurance Officer (QAO) and an alternate QAO. The two person team is designated as the Quality Assurance Unit (QAU). The QAO has primary responsibility for Quality Assurance activities; the alternate provides support when the QAO is not available. The QAU works in conjunction with the Branch Chief and the OPP Director of Quality Assurance (DQA) to ensure that the laboratory meets the specifications, goals, and objectives of the Quality Management Plan (QMP). The QAU reports directly to the MLB Branch Chief on administrative or technical matters. The Team Leader is responsible for the coordination of testing activities and technical support of analysts in the Laboratory. On quality assurance issues, the QAU reports directly to the OPP Director of Quality Assurance (DQA) and manages the laboratory's QA program with oversight provided by the DQA. The appointed QAU for the laboratory is responsible for determining whether all SOPs, QA/QC, and GLP requirements are met. The QAU is responsible for reviewing the quality of data and study reports, and conducts on-site audits and makes unscheduled visits for observations to assess whether the testing and general laboratory operations are carried out in accordance with approved SOPs. The QAU has access to the master schedule of testing activities and works in cooperation with the Team Leader to prepare an annual audit schedule. The OPP DQA is consulted before making final arrangements for these audits. The QAU maintains files of master copies of all SOPs, master schedules of testing activities, audit schedules, and records of audits and responses. The OPP DQA is responsible for final approval of the Quality Management Plan, and conducts Management System Reviews (MSRs) to ensure that QA activities are carried out according to the QA Management Plan.

Quality Assurance Project Plans (QAPPs) for new projects are developed as needed and are approved by the QAO or alternate. The type of plan will be dependent upon the work to be performed. Refer to the Appendix for the list of the QAPPs currently in place. The QAO is also responsible for preparing the laboratory's contribution to OPP's Quality Assurance Annual Report and Work Plan (QAARWP).

For Homeland Security projects, Senior Science Advisor serves as the Principal Investigator (PI) and has the overall responsibility for the technical conduct of the projects. Quality assurance issues are addressed in the laboratory through consultation of the QAO with the Team Leader, Senior Science Advisor and Branch Chief. Issues not amenable to resolution at this level are resolved between the DQA and Branch Chief. If resolution cannot be achieved, the matter is raised to the Divisional level.

V. Resource Allocation

Resources for the implementation of quality assurance practices in the laboratory are allocated on an annual basis. The laboratory has assigned a QAO and an alternate QAO, collectively known as the Quality Assurance Unit (QAU). The QAU attends Agency quality assurance training as well as other training provided by private entities. Other staff and analysts are also trained as the need arises and the resources are available. Traveling and training funds are set aside for this purpose on an annual basis. Capital investments are made to improve the quality assurance aspects of the laboratory program. If extramural resources are required,

suppliers must meet appropriate quality control and assurance requirements. Equipment calibration and certification by certified vendors is an integral part of the QA program.

C. QUALITY SYSTEM AND DESCRIPTION

I. Principal Components

The Agency's policy and program requirements to implement the mandatory QA programs are contained in EPA Order 5360.1A2. As stated in EPA Order 5360.1A2, "the primary goal of the QA program is to ensure that all environmentally related measurements supported by the EPA produce data of known and acceptable quality. The quality of data is known when "all components associated with its derivation are thoroughly documented, such documentation being verifiable and defensible." As of October 16, 1989, the Agency requires that efficacy studies performed by registered laboratories in support of submissions under FIFRA be conducted in compliance with Good Laboratory Practice (GLP) regulations.

The laboratory is charged with verification of efficacy claims of hospital disinfectants, including products which also make tuberculocidal claims. As enforcement actions may be taken based on the efficacy data generated by the laboratory, it is committed to producing data of known, acceptable, traceable, and defensible quality. In addition, data generated in other program areas is used to make recommendations which affect the regulation of pesticides, particularly antimicrobials and plant incorporated protectants (PIPs). The laboratory operates in conformance with GLPs and with a quality system in place with thorough documentation of all quality control measures to support the testing program.

The principal components of the laboratory's quality system are the Quality Assurance Management Plan, the Agency's Good Laboratory Practices, Standard Operating Procedures, Quality Assurance Projects Plans, and Study Protocols. Essential quality control measures are integrated into the SOPs which form the basis of laboratory operations. The SOPs are reviewed at least once every three years, and are revised as necessary. This promotes continual improvement of the SOPs and assessment of the adequacy of quality control requirements.

II. Process

The peer review and QAU review of all raw data and all final reports ensure that the quality control requirements are being met. Regular audits of general laboratory operations and performance of testing methods are also essential parts of the Laboratory's quality system. The QAO is responsible for conducting internal audits to determine whether SOPs are being used and followed correctly. The QAO also makes unannounced visitations to observe laboratory operations. These ongoing activities provide for continual assessment of the effectiveness of quality control procedures.

Audit reports are submitted by the QAO to the Team Leader and Branch Chief within the specified timeframe for completion of the audit. Responses must be returned to the QAO and

Branch Chief within an agreed upon timeframe. The Team Leader is responsible for addressing each finding or observation. A reason for the noncompliance, as well as a plan for corrective action, is required. If the QAO finds the corrective action deficient, the situation is discussed with the QA Manager for the Office of Pesticide Programs, the Team Leader and the Branch Chief. These procedures are detailed in Laboratory SOP QA-01, Quality Assurance Unit and its Functions.

Quality Assurance Project Plans (QAPPs) are developed as the need arises. Basic quality control principles are incorporated into QAPPs to ensure the integrity of the data generated and conclusions reached from special experimental studies.

For Homeland Security research projects, the preparedness of each participating laboratory, including the OPP Microbiology Laboratory, is assessed by the MLB Senior Scientist (or designee) and Quality Assurance Unit (QAU) prior to initiation of the study to ensure compliance with the Quality Assurance Project Plan and associated study protocol. Readiness reviews are conducted in advance of the initiation of research. The expected level of quality assurance is consistent with EPA Good Laboratory Practices. Numerous guidance documents, standard methods and SOPs are used to maintain data quality. Proper record keeping and archiving are performed to ensure the defensibility and reconstructibility or reanalysis of the study. Staff performing the assays must be familiar with standard microbiological techniques such as aseptic transfer, serial dilutions, plate counts and microbe identification. Scientists and analysts involved in testing shall be familiar with each efficacy method and associated procedure (e.g., carrier counts, neutralization confirmation) and will be proficient in conducting each designated efficacy test method. In-house practice sessions are required for each laboratory to build proficiency with each method prior to official testing. Documentation of practice and training for projects is maintained in a training file. Where possible, EPA SOPs and standard forms are used for those operations which have become or will become routine, including test methodology, analytical procedures and calibration procedures. SOPs that are comparable to EPA's may be used; however, their use requires concurrence by the Senior Scientist (or designee) or the EPA Quality Assurance Unit. Electronic spreadsheets and email are considered official documentation and will be maintained and archived accordingly. Test chemicals, media and reagents are tracked using assigned media preparation numbers. No official chain of custody documentation is required for test chemicals evaluated in Homeland Security research; however, specific information on source, identification, and volume received is maintained and archived. Upon completion of each study, a peer review of the data entry/tabulation is performed by laboratory personnel. A draft report of the findings or data summary is compiled and forwarded to each lab's Quality Assurance personnel for review. The designated QAO at each facility will review and comment on the data and supporting information before submission to the statistician. Data may be rejected if microbial contamination occurs at a level unacceptable to MLB.

D. PERSONNEL QUALIFICATIONS AND TRAINING

I. Policy

The Agency encourages the continued training, certification, and professional development of the laboratory staff to meet program objectives. Resources are allocated for these activities on a continuing basis.

II. Qualifications and Training

The work performed at the laboratory consists of microbiological and chemical assays. Analysts are required to use standard laboratory equipment, as well as new technology specific to the mission of the program. Analysts must meet the minimum qualifications set forth in Handbook 118 for microbiologists, or for biologists with a minimum of 20 semester hours in microbiology and related studies. Personnel job applications, curricula vitae, etc. are maintained by the Branch Chief. Job descriptions and training records for each employee, as specified under the GLPs Section 160.29(b), are available for inspection.

Student assistants and interns are required to have basic microbiology and chemistry courses at the college level. On-the-job training will be provided to each student by senior laboratory personnel on laboratory specific practices and procedures. Students may work independently on assigned research projects with direction and guidance from the laboratory team leader or senior scientist.

All laboratory staff is required to have 24 credits of general laboratory safety training as specified under the Agency guidelines. A refresher class of 8 credits is required on an annual basis. If specific personal protective equipment such as respirator is required, the analyst must be certified.

The laboratory staff is trained in laboratory operations through review of SOPS, QA/QC requirements, chain-of-custody procedures, and record keeping requirements. New staff members receive extensive hands-on training from the Team Leader or senior analysts on methods and procedures used in the laboratory. Staff obtains experience by performing practice trials including handling of cultures, disinfectants, chemicals, etc. The Quality Assurance Officer provides training on various aspects of quality control procedures. Methods related to safety and health practices are also covered by the ESC Industrial Hygienist and the facility safety officer. Training by the vendors of microbiology laboratory equipment is conducted as needed. QA training is recorded in the training file for each employee.

For professional development, analysts are encouraged to attend seminars and professional meetings such as those of the American Society for Microbiology (ASM), Association of Official Analytical Chemists (AOAC) International, Association of Practitioners for Infection Control (APIC) and Analytical Excellence through Industry Collaboration (AEIC), etc. Information on new equipment is obtained through trade journals, trade shows, and vendor

demonstrations. Specific training needs related to successful performance of laboratory duties, available through AOAC International, the National Institutes of Health (NIH), the US Food and Drug Administration, state laboratories, or other organizations, may be identified and submitted as training requests. Funding for training is allocated during the annual budget planning process.

The Agency, through its Office of Environmental Information Quality Staff, provides basic training courses in quality assurance for Quality Assurance Officers. BEAD management supports the QA program by providing funding for training and travel. BEAD allocates funding for the QAO to participate in EPA's annual QA conferences.

III. Proficiency Testing/Uncertainty

In order to determine intra-laboratory variability and the expertise of the analyst in performing certain functions, the laboratory is currently developing a proficiency program. Tasks that will be evaluated include basic microbiology laboratory tasks such as dilution plating, reading of results and recording of data. The Team Leader will be responsible for implementing the program and evaluating the results. Assistance from the QAO will be provided as necessary to ensure the quality of data. Refer to the "OPP Microbiology Laboratory Response to the EPA Laboratory Competency Policy Directive, Implementation Plan", Reference #5.

For the PIP method validation program, the laboratory participates in the USDA Grain Inspection, Stockyards and Packers Administration (GIPSA) proficiency program for the detection of biotechnology events. Blind samples are sent to the laboratory for screening. The laboratory returns the data to GIPSA for analysis, and the results are posted for each laboratory.

For the Homeland Security research, quality assurance readiness reviews and in-house practice sessions are used to develop and monitor proficiency in conducting microbiological techniques associated with test methods prior to the initiation of the research.

MLB recognizes the importance of uncertainty of measurement, or error, associated with the lab's activities. Where possible, certified media and reagents and specialized equipment (e.g., specific types and sizes of pipettes, volumetric glassware) are used in the laboratory's assays. Rigorous quality assurance, staff training, and calibration of equipment such as balances, pH meters and spectrophotometers are used to increase reproducibility of data. Equipment for quantitative assays such as positive displacement pipettes and cuvettes are performance tested and validated by the manufacturer. Quantitative efficacy tests are replicated by the laboratory to provide within-lab standard deviation values, or when necessary, are performed by more than one laboratory to provide between-lab standard deviation values. The laboratory utilizes AOAC-validated methods for the ATP program and is seeking third-party validation of new methods under the Homeland Security initiative. Furthermore, charting of quantitative data such as carrier counts is used to monitor the outcome of laboratory methods.

E. EXTRAMURAL AGREEMENTS AND PROCUREMENT OF ITEMS AND SERVICES

As part of an internal quality control program, the laboratory verifies the quality of the deionized water used in making media, reagents, and to dilute disinfectants during efficacy testing. As discussed in the laboratory Standard Operating Procedure (SOP) for quality assurance of purified water, de-ionized water is checked for total heavy metals, specific heavy metals (Cadmium, Lead, Nickel, Zinc, Copper, and Chromium), ammonia and organic nitrogen (Total Kjeldahl Nitrogen), total organic carbon, conductivity, total chlorine residual, heterotrophic plate counts, and water suitability. Monitoring of total chlorine residual is performed on a monthly basis by the EPA/OPP Microbiology Laboratory. Monitoring of total heavy metals, specific heavy metals, total organic carbon, conductivity, heterotrophic plate counts, and water quality is performed by QC Inc. laboratory (1205 Industrial Blvd., Southampton, PA 18966-0514, 215-355-3900). QC Inc. is certified by the State of Maryland Department of Health and Mental Hygiene Laboratories Administration as a State Certified Water Quality Laboratory. Monitoring of Total Kjeldahl Nitrogen is performed by NASA Environmental Science Laboratory Services (Building 8110/Room 102, Stennis Space Center, MS 39529, 228-688-1039). NASA Environmental Science Laboratory Services is certified by the Mississippi State Department of Health's Public Health Laboratory as a certified drinking water laboratory. Following each round of sample analysis, Vendors forward the analytical results to the OPP Microbiology laboratory. The laboratory staff analyzes the results as described in the SOP.

Laboratory balances, weights, timers, NIST-traceable thermometers, hygrometers, and spectrophotometers are certified by contract vendors on an annual basis to ensure accuracy. The Vitek 32 and Vitek 2 Compact systems, for automated identification of microorganisms and Pipettes (Rainin) are factory certified and are serviced annually. ELISA reader verification plates are sent out for traceable certification every two years. Preventative maintenance on large equipment, including biological safety cabinets (BSCs), fume hoods, and autoclaves is provided by the building's Facility Manager. The Facility Manager utilizes outside vendors to service these pieces of equipment and to annually certify the BSCs and fume hoods. In-house calibration procedures and frequencies for other apparatus used in the laboratory are detailed in the appropriate Equipment (EQ) and Quality Control (QC) SOPs.

For Homeland Security-related projects, the following extramural agreements have been established:

- Interagency Agreements (IAGs) with U.S. Army Edgewood Chemical and Biological Center (ECBC), Aberdeen Proving Ground, MD, and the U.S. FDA (Denver District Laboratory, Winchester Engineering and Analytical Center Laboratory, White Oak Campus Laboratory) have been developed to provide funding for personnel resources and the equipment and supplies expended or consumed during the project. ECBC and FDA provide expertise and technical support in the collaborative testing of test methods, surrogates, and decontamination chemicals.

- An IAG with FDA (pre-existing contract with AOAC) is being used to fund AOAC International for services through FY07 to validate selected test methods and/or method modifications for sporicides.
- Collaborative research with ORD's National Homeland Security Research Center, Cincinnati, OH; MLB contributes Homeland Security funding to ORD to support test method and surrogate studies conducted by Battelle (contractor).
- Contract with the North Carolina Department of Agriculture laboratory to provide disinfectant efficacy testing of EPA registered hospital disinfectants.
- Dr. Martin Hamilton, Professor of Statistics, Montana State University, is the statistician current assisting MLB on the Homeland Security projects. Dr. Hamilton's services were funded through a contract with OPP's Antimicrobials Division (MLB contributed funding to the contract).
- Inoculated porcelain penicylinders and spore suspensions are purchased from Presque Isle Cultures, 3804 West Lake Rd., P.O. Box 8191, Erie, PA 16505.

Other Assistance Agreements

In addition, the Ohio Department of Agriculture and Michigan Department of Agriculture are supported by State and Tribal Assistance Agreements to provide antimicrobial efficacy data under the Antimicrobial Testing Program. Each of the laboratories has a Quality Management Plan or a Quality Assurance Project Plan which identifies the systems in place to ensure the quality of the data. MLB reviews each of the efficacy reports submitted by the state laboratories to ensure consistency with program objectives.

F. DOCUMENTS AND RECORDS

I. Process for Recording and Maintaining Data

The laboratory Standard Operating Procedures (Appendices A5 and A6) have forms for documenting laboratory data and supporting information. Certain information may be documented using prepared data recording forms; these forms were developed to maintain consistency in recording of information and to provide a pre-established report format to clients.

The data from analyses of samples and the data from the ongoing QA/QC activities are reviewed by the analysts. Whenever the internal quality control checks or audits indicate non-conformance to accepted protocols and procedures, corrective action is taken. The vast majority of ATP data are qualitative in nature. For those methods which require construction of charts, standard curves, plotting survivors vs time as in the Quantitative Suspension Test Method

(QSTM), the curves would be developed as described in the method and as reflected in the SOP. For quantitative tests, log reduction estimates are calculated using spreadsheet software. Standard curve and calibration data generated for Enzyme-linked Immunosorbent Assay (ELISA) method validations are analyzed using Ascent Software provided with the Multiskan Ascent microplate reader.

Test data will be recorded manually or automatically through computer/ instrument interfaces. A complete audit trail will follow any entry. Original copies of any hand-written results will be maintained.

For the Antimicrobial Testing Program reports, the draft report is peer reviewed and then procedures are followed as specified in the SOP for generation of a final report to the client. Other reporting mechanisms may be used to report findings from laboratory studies dependent on the needs of the client. The laboratory stores the draft performance report, the final performance report, and associated memoranda in individual labeled containers by product. All raw data, performance reports and quality control records are maintained in the archive room. Records are retained in the designated space at the ESC for the length of time listed in the laboratory's retention schedule. Records are archived as specified in the retention schedule.

II. Quality Assurance Records

Records of routine quality control activities are recorded in laboratory notebooks. In accordance with GLP's, the laboratory's quality control practices include thorough documentation of laboratory operations; the original documents are kept on file as specified in the SOP

Copies of all audit reports are archived. The MLB Branch Chief, or designated staff shall be responsible for the files in the event of the QA Officer's absence. In addition, the QAO maintains electronic copies of all memoranda related to QA activities. The Branch Chief shall have keys for access to these files.

III. Archives and Disposition

The retention schedule for the Laboratory documents is contained in the SOP for Records and Archives. The records retention schedule is consistent with the U.S. EPA Records Control Schedule. Records will be retained in the laboratory for the length of time listed in the file plan unless volume warrants a transfer to a records archive area. When the retention time for a set of records has passed, the records will be destroyed. All records formerly housed at the Cincinnati testing facility and generated at the ESC have been retained and will be subject to the official records retention schedule.

The location of these records is in a secured room at the ESC. Individual files are kept in filing cabinets within this room. The QAO, Team Leader, Senior Science Advisor, Branch Chief and authorized analysts shall have access to these filing cabinets.

G. COMPUTER HARDWARE AND SOFTWARE

The Vitek 32 and Vitek 2 Compact, automated identification Systems for microorganisms, are used in the laboratory for confirmatory organism identification. Software for the systems are upgraded when necessary during annual maintenance. Personal computers are programmed, monitored, and serviced by technical staff from OPP and Region III and meet all Agency requirements for security, technical requirements and quality expectations.

An ESC facility-wide Chemical Inventory Management System (ChIM® by Vertere) is used by the OPP Microbiology Laboratory to track reagents and media. Functionality of the System includes: Chemical Identification, Individual Item tracking, Safety Data, and Inventory History. The chemical inventory management system, or ChIM, enables users to search a database to determine if a needed chemical is already present in the laboratory. The software meets the Agency's standards.

The laboratory has developed an automated system for maintaining an inventory and tracking expiration dates for laboratory chemicals, reagents, and other materials in Access. The laboratory will use standard Agency software (Access, Excel) to chart certain information such as carrier counts, media performance etc., in order to identify outlier data points and information. Results obtained by the laboratories involved in the Antimicrobial Testing Program are being entered into an Oracle database so that trends or unusual findings can be monitored.

H. PLANNING

In FY 2007, the laboratory will continue with antimicrobial efficacy initiatives, additional PIP method validations, ORD Homeland Security funded sporicidal research, and efficacy method research and development. Antimicrobial product testing will continue at the laboratory although it is anticipated that the state laboratory program will be responsible for a large portion of the hospital disinfectant testing. Laboratory projects are captured on the OPP Microbiology Laboratory Branch FY 2007 Annual Workplan. New initiatives are reviewed and approved at the division director level. The laboratory works closely with the client base in the development of the yearly work plans to ensure that the laboratory projects mesh with the needs of the regulatory programs. Several new projects are anticipated during the fiscal year which expand and enhance the capabilities of the laboratory including the development of viral capabilities, biofilm assays, and work with new and emerging pathogens.

For new projects outside the regular core programs, such as research projects or collaborative exercises, the laboratory will develop a QAPP for each project. The QAPP will include the necessary criteria such as project manager, goals, schedule, type of data to be generated, performance measures, QA/QC activities, audits, requirements for analysis of data, appropriate statistical measures, and other parameters necessary to ensure the validity and reliability of the data. Each Quality Assurance Project Plan will be reviewed and approved by

the laboratory's Quality Assurance Officer prior to initiating the project.

Annual, internal technical and system audits will be conducted by the QAO based on the testing/research schedule of the laboratory and any issues identified through prior audits. These audits will be both scheduled and unannounced. The tentative schedule will be developed by the QAO and Team Leader in January of each year and adjusted to accommodate events such as changes in sample collection receipts or new collaborative testing.

The laboratory will request audits from external sources annually. These audits may cover technical, management system, and GLP reviews. The Laboratory will consult with the OPP Director of Quality Assurance in scheduling these audits.

I. IMPLEMENTATION OF WORK PROCESSES

The senior management for the program is responsible for ensuring that the work is implemented according to the developed schedule and plan. As operations or priorities change, the management will identify the critical processes that are necessary to ensure the validity of the data. If the changing priorities require the development of new SOPs, revisions to the QMP, or implementation of QAPP's, the management is responsible for the development of the necessary quality assurance practices. Any change which may impact the quality of the data generated by the laboratory will be done formally through the QAO.

The current Standard Operating Procedures for the laboratory are assigned control numbers. The laboratory's quality assurance officer is responsible for assigning the control copy numbers. If changes are made the QAO will verify that revisions are appropriate, that the review and signature procedures are followed, and the previous version is appended, or retired and the new SOP is put into practice.

The laboratory Team Leader is responsible for the development of the product testing schedule. If the work is interrupted or unanticipated problems occur, he/she will revise the schedule accordingly. The laboratory Senior Scientist is responsible for the technical direction of the laboratory programs and provides oversight and technical guidance to the laboratory scientists.

The laboratory will request audits from external sources periodically. These audits may cover technical, management system, and GLP reviews. The laboratory will consult with the OPP Director of Quality Assurance in scheduling these audits

J. ASSESSMENT AND RESPONSE

The generation of quality data is the responsibility of each laboratory employee. Each individual on the laboratory team is trained on the use of laboratory equipment, quality control practices, characteristics of the microorganisms, confirmatory techniques, recording of data elements, appropriate means of correcting any entry errors, and other daily operational activities

which may impact the validity of the generated data. Adherence to appropriate quality control and quality assurance activities is identified as an critical element in each laboratory employee's performance standard.

A preliminary quality assurance check of the data sheets is performed by a member of the laboratory team not assigned to the assay being performed. Once the check has been done, the report is compiled and directed to the Team Leader, then to the QAO as outlined previously.

The quality assurance officer will review the results of proficiency testing, once the program is developed, with the laboratory Team Leader and make recommendations for follow-up action if required.

The QAO has authority to audit any laboratory data or practices. Any deficiencies will be brought to the attention of the Team leader and Branch Chief and immediate action will be taken to correct the deficiencies. The QAO will recommend external audits as appropriate. These audits are typically done with a team of Agency scientists with expertise in microbiology and chemistry. The audit team presents the results to the laboratory management and corrective action is the responsibility of the senior management team.

K. QUALITY IMPROVEMENT

The current practices and activities identified in the QA management plan work to ensure the validity and reliability of the data generated by the laboratory. The internal audits, external audits, and review schedule of the SOPs provide opportunities for assessment and improvement of the quality systems. Communications between the laboratory team, quality assurance officer, and management encourage the exchange of information which is necessary to improve ongoing activities. The team meets on a regular basis to exchange information and to make improvements to data forms, SOPs, and facility practices. The team is integrating automation into the current practices. The team also interfaces with laboratory customers and support services to share information and exchange ideas.

L. REFERENCES

1. OPP Microbiology laboratory ATP-QAPP-2004-01
2. OPP Microbiology laboratory PIP-QAPP-2004-01
3. OPP Microbiology laboratory ORD Safe Buildings Program QAPP-2003-01
4. OPP Microbiology Laboratory Fiscal Year 2007 Workplan
5. OPP Microbiology Laboratory Response to the EPA Laboratory Competency Policy Directive, Implementation Plan

M. LIST OF APPENDICES

Appendix A-1 Organizational Chart – Office of Pesticide Programs

Appendix A-2 Biological and Economic Analysis Division

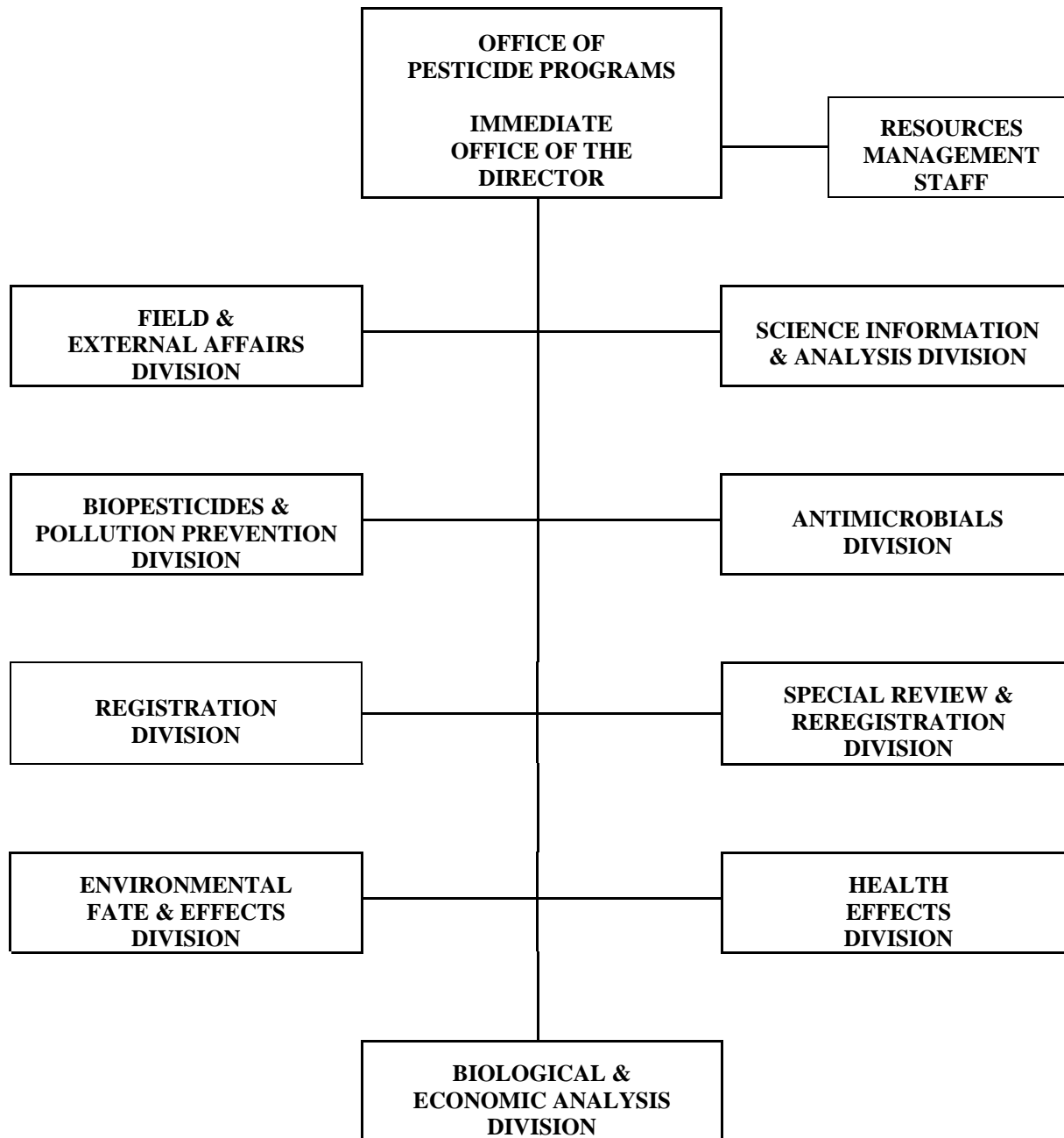
Appendix A-3 Organizational Scheme: QAPP 2003-01

Appendix A-4 Organizational Scheme: QAPP 2004-01

Appendix A-5 Index of ATP Standard Operating Procedures

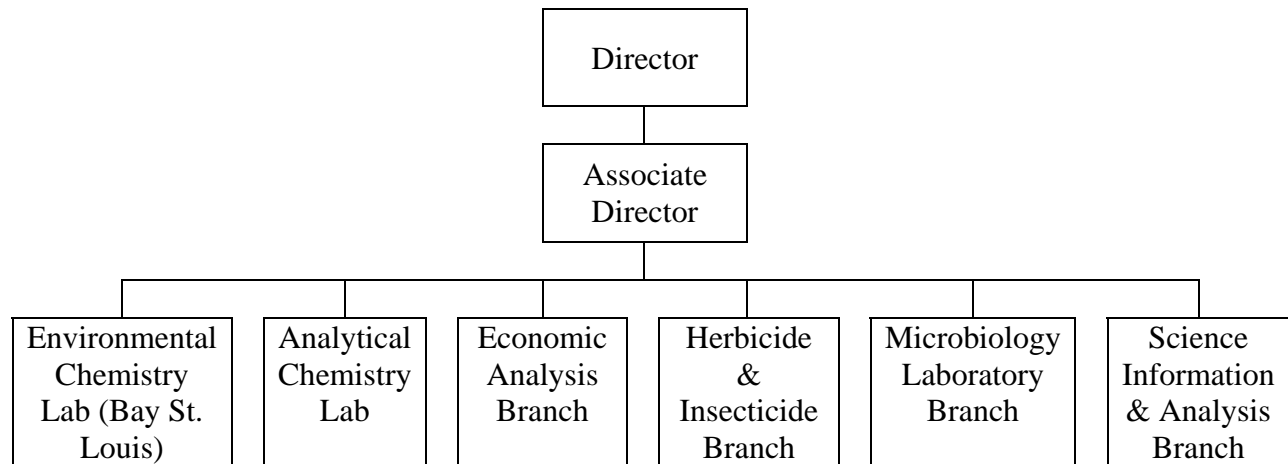
Appendix A-6 Index of PIP Standard Operating Procedures

**APPENDIX A-1
ORGANIZATION OF OPP**



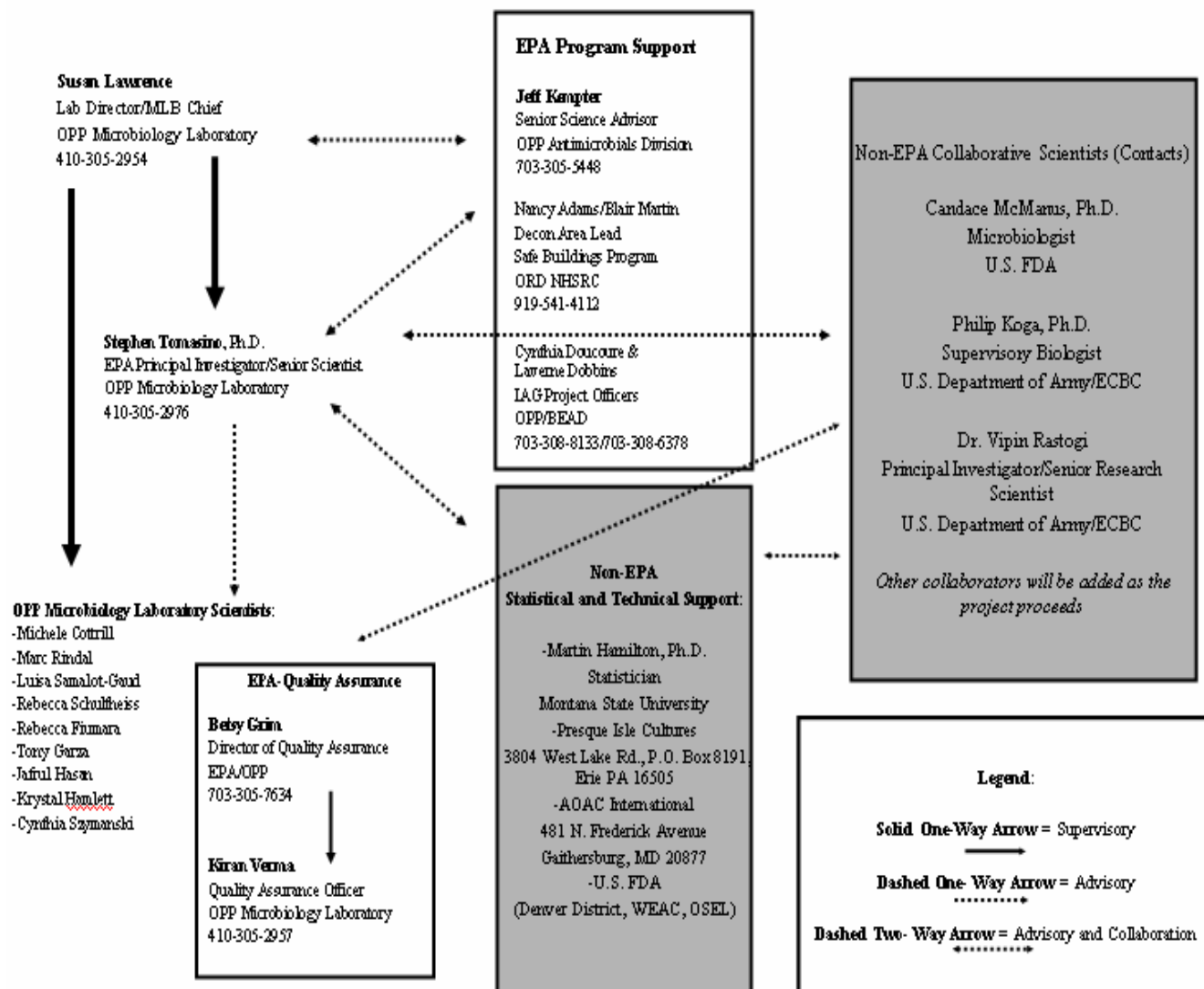
APPENDIX A-2

ORGANIZATION OF BIOLOGICAL AND ECONOMIC ANALYSIS DIVISION



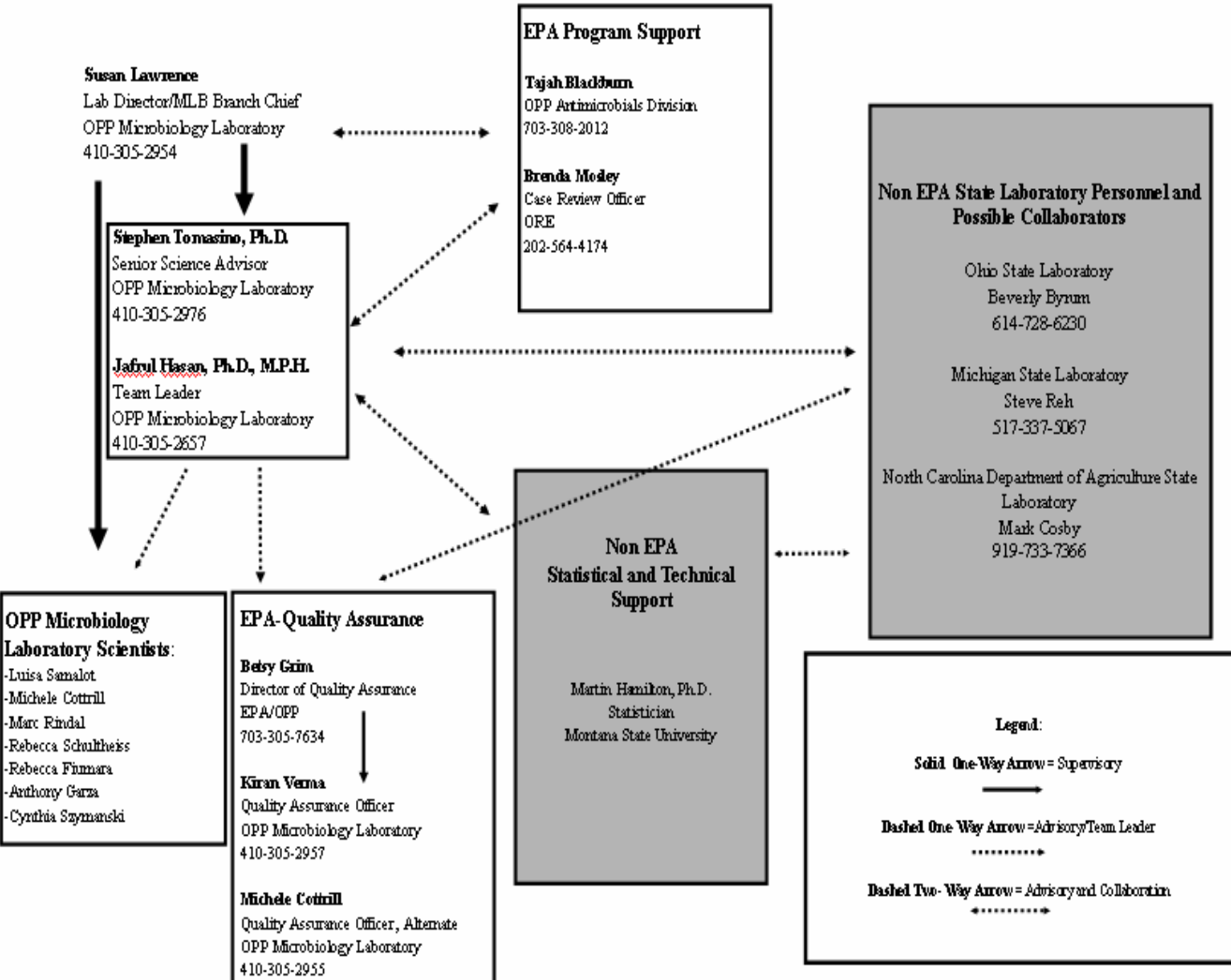
APPENDIX A-3

Organizational Chart QAPP No. 2003-01



APPENDIX A-4

US EPA-OPP Microbiology QAPP 2004-01



APPENDIX A-5
Index of ATP Standard Operating Procedures
OPP Microbiology Laboratory

Antimicrobial Testing Program SOPs	
SOP	Title
EQ-01-04	Calibration and Maintenance of pH Meters
EQ-02-03	Calibration of Thermometers
EQ-03-03	Calibration and Maintenance of Weigh Balances
EQ-04-03	Systems Check for the Beckman (DU Series 500) Spectrophotometer
EQ-05-03	Calibration and Maintenance of Timers
EQ-06-03	Calibration of Kimble Class A Burets
EQ-08-03	Verification of Volume Dispensed and Maintenance of Oxford Automatic Dispenser and Hamilton Microlab 500
MB-01-04	Biosafety in the Laboratory
MB-02-03	Test Microbes for the AOAC Use-Dilution Method, AOAC Germicidal Spray Product Test, Germicidal Towelette Product Test, AOAC Confirmatory Tuberculocidal Test, and the AOAC Sporocidal Activity Test Method: Culture Initiation, Culture Maintenance and Quality Control
MB-03-03	Screening Carriers Used in Disinfectant Efficacy Testing
MB-04-03	Determining Carrier Counts
MB-05-04	AOAC Use Dilution Method for Testing Disinfectants
MB-06-02	Testing of Spray Disinfectants Against <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , and <i>Mycobacterium bovis</i> (BCG)
MB-07-03	Confirmatory Tuberculocidal Method for Testing Disinfectant Efficacy
MB-10-02	Media and Reagents Used in Efficacy Testing of Disinfectants
MB-11-01	Neutralization Confirmation Assay for Disinfectant Products Tested Against <i>Mycobacterium bovis</i> BCG
MB-12-01	Neutralization Confirmation Procedure for Products Evaluated with the AOAC Sporocidal Activity Test (<i>Bacillus</i> Species)
MB-13-00	Handling Spills of Biohazardous Material
MB-15-00	AOAC Sporocidal Activity Test (<i>Bacillus</i> Species)
MB-16-00	Quantitative Suspension Test Method for Determining Tuberculocidal Efficacy of Disinfectants Against <i>Mycobacterium bovis</i> (BCG)
MB-17-00	Neutralization Confirmation Procedure for Products Evaluated with the AOAC Use Dilution Test and the AOAC Germicidal Spray Product Test (<i>Staphylococcus aureus</i> and <i>Pseudomonas aeruginosa</i>)
MB-18-00	Use and Operations of the Receiving Room (D122)
QC-01-03	Quality Assurance of Purified Water
QC-02-02	Air/Surface Monitoring of Microbiology Laboratories (Retired 10/27/05)
QC-03-04	Glass Washing and Detergent Residues Test

Antimicrobial Testing Program SOPs	
SOP	Title
QC-04-02	Cleaning and Disinfection of Recirculating Chillers (Retired 10/25/05)
QC-05-03	Monitoring Temperature of Incubators, Refrigerators, and Freezers
QC-06-03	Use and Maintenance of Biological Safety Cabinets
QC-07-02	Monitoring Water Temperature of Recirculating Chillers (Retired 10/25/05)
QC-08-03	Monitoring Temperature/Humidity of the Sample Storage Room
QC-09-03	Establishment of Control Numbers and Tracking Laboratory Supplies
QC-10-03	Media and Reagents: Examination and Expiration Time
QC-11-02	Performance Assessment and Sterility Verification of Prepared Media and Reagents
QC-12-02	Sterility Check of Pre-Sterilized and Autoclaved Laboratory Supplies (Retired 11/30/04)
QC-13-03	Performance Verification of Autoclaves
QC-14-03	Monitoring Temperature of Water Baths for Holding (Tempering) Media
QC-15-03	Media and Reagent Preparation: Assigning Prep and Sterilization Run Numbers
QC-16-03	VITEK: Establishment of Culture Identification Numbers
QC-17-03	VITEK: Quality Control Procedures
QC-18-03	Sterility Assessment of Disinfectant Product Samples
QC-19-03	Calibration of Eppendorf Pipettes Using the PCS 2 Pipette Calibration System
QC-20-02	Autoplate 4000 Automated Spiral Plater (Retired 10/25/05)
QC-21-00	Use of the AOAC Use Dilution Test and the Germicidal Spray Products Test without Test Microbes to Determine the Presence of Microbial Contamination in EPA-Registered Hospital Disinfectants
QC-22-00	VITEK 2 Compact: Use, Maintenance and Quality Control Procedures
ADM-01-02	Preparation and Review of Disinfectant Performance Reports
ADM-02-02	Preparation and Review of Standard Operating Procedures (SOPs)
ADM-03-02	Records and Archives
ADM-04-01	OPP Microbiology Laboratory Training Program
ADM-05-00	Guidelines for Use and Maintenance of Laboratory Notebooks and Project Binders
COC-01-03	Disinfectant Sample Login and Tracking
QA-01-03	Operations of the Quality Assurance Unit
QA-02-02	Internal Quality Assurance Audits (Retired-Combined with QA-01)
QA-04-02	Master Schedule Preparation

APPENDIX A-6
Index of PIP Standard Operating Procedures
OPP Microbiology Laboratory

Plant Incorporated Protectant Method Validation Program SOPs		
01	PIP-ADM-01-00	Use of Laboratory Notebooks
02	PIP-COC-00	Plant Incorporated Protectant Method Validation Program Login and Tracking of Technical Materials
03	PIP-EQ-01-00	Performance Verification of the GeneAmp PCR System 9700
04	PIP-EQ-02-00	Performance Verification of PCR Amplification in the PE Biosystems GeneAmp PCR System 9700
05	PIP-EQ-03-00	Performance Verification and Maintenance of the Microplate Photometer
06	PIP-EQ-04-00	Operation and Maintenance of the Eppendorf Centrifuge Model 5804R
07	PIP-EQ-05-00	Operation and Maintenance of the Labsystems Wellwash 4 Mk 2 Automatic Microplate Washer
08	PIP-EQ-06-00	Use and Maintenance of the Rainin Single Channel Pipettes, Multi-channel Pipettes, and Repeater Pipette
09	PIP-EQ-07-00	Use and Maintenance of the Polytron PT 3100 Laboratory Homogenizer
10	PIP-MB-01-00	Workflow Through the Laboratory
11	PIP-MB-02-00	Conducting a Method Validation Pre-Review